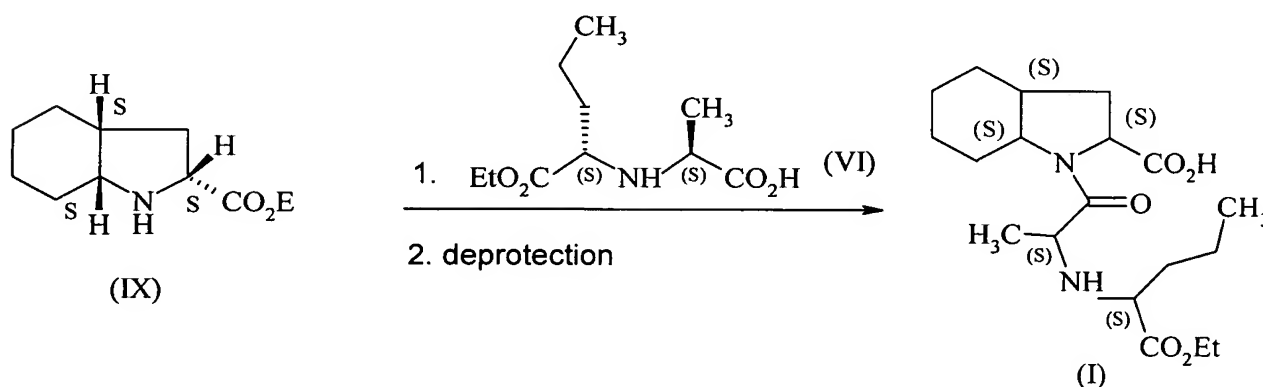


REMARKS

The Applicants acknowledge the Examiner's comprehensive Office Action with appreciation. Claims 7-12 remain pending in the application. The Office raises a rejection under 35 USC § 102 as well as an obviousness-type double patenting rejection. The Office also acknowledges the Information Disclosure Statement filed with the filing papers of the instant application.

Claims 7-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 7-12 of co-pending application US Serial No. 10/582,283. With this Response and Amendment, the Applicants submit a Terminal Disclaimer, thereby obviating the rejection.

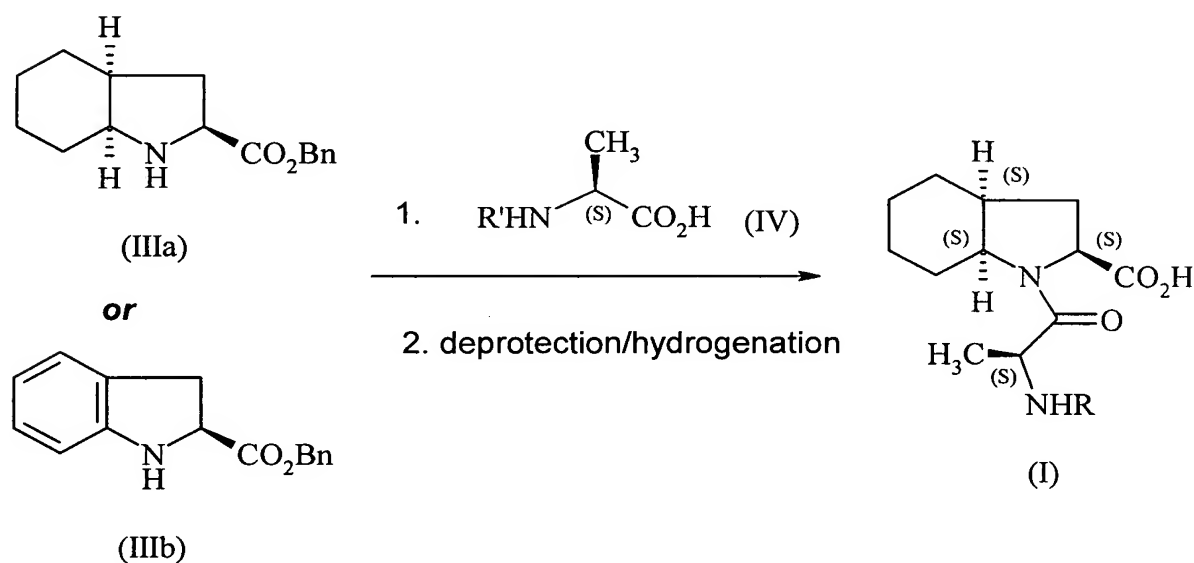
Claims 7, 8, 10, and 12 are rejected under 35 USC § 102(b) as being anticipated by Vincent, et al. It is the position of the Office that Vincent, et al. disclose a process for the synthesis of perindopril which involves reaction of a compound of formula (IX) (wherein E represents lower alkyl or benzyl) with a compound of formula (VI) in the presence of a catalyst for peptide synthesis, such as dicyclohexyldicarbodiimide in the presence of 1-hydroxybenzotriazole, followed by deprotection of the resulting compound to yield perindopril of formula (I):



It is the further position of the Office that Vincent, et al. disclose specific reaction conditions involving removal of the benzyl protecting group via catalytic hydrogenation. Therefore, the Office concludes that the process disclosed in

Vincent, et al. anticipates the instantly claimed process which utilizes a compound of formula (IIa).

The instant application has claims directed to a process for the synthesis of compounds of formula (I) (i.e., an intermediate for use in the synthesis of perindopril), which process involves reaction of a compound of formula (IIIa) or (IIIb) with a protected alanine derivative of formula (IV) followed by a deprotection/hydrogenation step:



The instant application also has claims directed to a process for the synthesis of perindopril, which process involves further elaboration of the N-substituent of indoline ring of the compound of formula (I).

The Applicants respectfully submit that, in contrast to the process disclosed in Vincent, et al. which involves coupling of two components (i.e., the indoline ring and the N-substituent of the indoline ring) followed by a hydrogenation/deprotection step to yield perindopril as the final product, the instantly claimed process involves coupling of two components (i.e., the indoline ring and a protected alanine derivative) followed by a hydrogenation/deprotection step to produce an

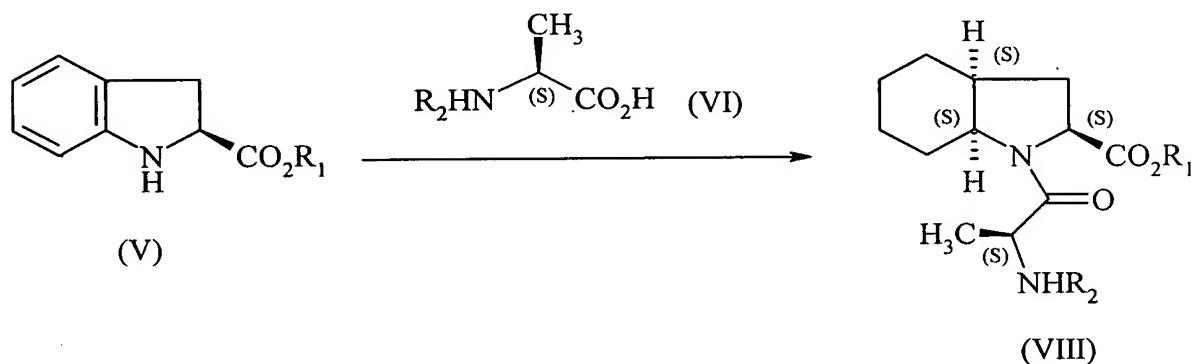
intermediate, which intermediate may then be converted to perindopril via further elaboration of the N-substituent of the indoline ring.

Moreover, in the compound of formula (VI) of the Vincent, et al. process, the moiety corresponding to the R' substituent of instant formula (IV) is an ethyl pentanoate moiety. With the instant amendment, the R' substituent of instant formula (IV), which serves as a protecting group for the amino function, has been further defined to recite specific protecting groups (i.e., tert-butyloxycarbonyl, benzyl, and benzyloxycarbonyl). Support for this amendment may be found at page 5 of the instant specification. Thus, the compound of formula (VI) of the Vincent, et al. process is clearly not encompassed by the compound of formula (IV) of the instantly claimed process.

Therefore, the Applicants respectfully submit that the instant process is not anticipated by the process disclosed in Vincent, et al.

Claims 7-9 and 11 are rejected under 35 USC § 102(e) as being anticipated by Mezei, et al. (US Patent No. 7,060,842). It is the position of the Office that the instantly claimed process which utilizes the benzyl ester of formula (IIIb) is anticipated by the process disclosed in Mezei, et al.

Mezei, et al. disclose a process for the synthesis of compounds of formula (VII) which are useful in the synthesis of perindopril (wherein R₁ of the compound of formula (V) may represent benzyl and wherein R₂ of the compound of formula (VI) represents a protecting group).



The process disclosed in Mezei, et al. utilizes dicyclohexyldicarbodiimide or dicyclohexyldicarbodiimide/1-hydroxybenzotriazole as the coupling agent in amounts which provide the compound of formula (VIII) which is substantially free of contaminations resulting from dicyclohexyldicarbodiimide. Mezei, et al. further disclose that the specific reaction conditions are critical to the purity of the perindopril final product.

The instantly claimed process does not utilize the specific coupling agents (i.e., dicyclohexyldicarbodiimide alone or dicyclohexyldicarbodiimide/1-hydroxybenzotriazole) which are used in the Mezei, et al. process. Therefore, the Applicants respectfully submit that the instant process is not anticipated by the process disclosed in Mezei, et al.

Reconsideration and withdrawal of the anticipation rejections under 35 USC § 102 is respectfully requested.

Finally, Claim 7 has also been amended to correct certain typographical errors, i.e., the term (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide has been replaced with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

* * * * *

Accordingly, entry of present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned agent has made an earnest effort to place this application into condition for immediate allowance. If she can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call her at her below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

By: 
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Enclosure: Terminal Disclaimer and Fee (Check No. 75589) under 37 CFR §
1.20(d); Listing of Claims; and Postal Card Receipt

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**THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER
OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION,
DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO
DEPOSIT ACCOUNT NO. 08,3220.**